6,472,585, which is a continuation of U.S. Application Serial No. 09/234,730, filed January 21, 1999, which is a continuation-in-part application of U.S. Application Serial No. 09/033,114, filed March 2, 1998, which is a continuation of U.S. Application Serial No. 08/733,850, filed October 18, 1996, now abandoned, which is a continuation of U.S. Application Serial No. 08/443,129 filed May 17, 1995, issued May 6, 1997 as U.S. Patent No. 5,627,073, which is a divisional of U.S. Application Serial No. 08/286,304 filed August 5, 1994, issued November 5, 1996 as U.S. Patent No. 5,571,893, which is a continuation-in-part of U.S. Application Serial No. 08/233,609 field April 25, 1994, issued July 9, 1996 as U.S. Patent No. 5,534,615, and to U.S. Provisional Application Serial No. 60/113,296, filed December 22, 1998, the entire disclosure of which is hereby incorporated by reference.

Please replace the paragraph beginning at page 4, line 23, with the following rewritten paragraph:

Figures 1A and 1B (SEQ ID NO: 1 and 2) show the nucleotide sequence of DNA58125 beginning in Figure 1A and continuing onto Figure 1B. DNA58125 is a cDNA encoding a native sequence cardiotrophin-1 (CT-1). SEQ ID NO:1 is the coding strand of DNA58125 and SEQ ID NO:2 is the complementary strand of DNA58125. SEQ ID NO:3, shown in Figure 1A, is the derived amino acid sequence of a native sequence cardiotrophin-1 (CT-1).

Please replace the paragraph beginning at page 7, line 32, with the following rewritten paragraph:

As used herein, the terms a "CT-1" polypeptide is used to refer to a polypeptide comprising a native sequence polypeptide having the same amino acid sequence as a corresponding CT-1 polypeptide derived from nature, and fragments of such native sequence polypeptides. Such native sequence CT-1polypeptides can be isolated from nature or, along with the respective fragments, can be produced by recombinant and/or synthetic means. The term specifically encompasses naturally-occurring truncated or secreted forms (*e.g.*, an extracellular domain sequence), naturally-occurring variant forms (*e.g.*, alternatively spliced forms) and naturally-occurring allelic variants of the CT-1

C3

polypeptide. In one embodiment of the invention, the native sequence CT-1 is a full-length native presequence or a mature form of a CT-1 polypeptide shown in Figure 1A (SEQ ID NO:3). Fragments of the respective native polypeptides herein include, but are not limited to, polypeptide variants from which the native N-terminal signal sequence has been fully or partially deleted or replaced by another sequence, and extracellular domains of the respective native sequences, regardless whether such truncated (secreted) forms occur in nature.

Please replace the paragraph beginning at page 52, line 20, with the following rewritten paragraph:

C4

DNA comprising the coding sequence of full-length or mature CT-1 (as shown in Figures 1A and 1B, SEQ ID NOs:1 and 2) is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of CT-1) in human tissue cDNA libraries or human tissue genomic libraries.

Please replace the paragraph beginning at page 21, line 10, with the following rewritten paragraph:

C5

According to the present invention, such genes have been identified by quantitative PCR (S. Gelmini *et al.*, Clin. Chem. 43, 752 [1997]), by comparing DNA from a variety of primary tumors, including breast, lung, colon, prostate, brain, liver, kidney, pancreas, spleen, thymus, testis, ovary, uterus, etc. tumor, or tumor cell lines, with pooled DNA from healthy donors. Quantitative PCR was performed using a TAQMAN® PCR instrument (ABI). Gene-specific primers and fluorogenic probes were designed based upon the coding sequences of the DNAs.

Please replace the paragraph beginning at page 38, line 16, with the following rewritten paragraph:

C6

The starting material for the screen was genomic DNA isolated from a variety of cancers. The DNA is quantitated precisely, *e.g.* fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5'

nuclease assay (for example, TAQMAN® PCR) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding CT-1 is over-represented in any of the primary lung or colon cancers or cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 1. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 1 and the primary tumors and cell lines referred to throughout this example has been given hereinbefore. The results of the TAQMAN® PCR are reported in delta (Δ) Ct units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a TAQMAN® PCR fluorescent prove derived from the CT-1-encoding gene. Regions of CT-1 which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are preferred for the primer and probe derivation, *e.g.* a 3'-untranslated region. The sequences for the primers and probes (forward, reverse and probe) used for the CT-1 gene amplification were as follows:

C6

CT-1 (DNA58125):

58125.tm.f1

5'-TTCCCAGCCTCTCTTTGCTTT-3' (SEQ ID NO: 4)

58125.tm.r1

5'-TCAGACGGAGTTACCATGCAGA-3' (SEQ ID NO: 5)

58125.tm.p1

5'-TGCCCCGTTCTCTTAACTCTTGGACCC-3' (SEQ ID NO: 6)

Please replace the paragraph beginning at page 43, line 18 with the following rewritten paragraph:

C7

The fluorometricly determined concentration was then used to dilute each sample to 10 ng/μl in ddH_2O. This was done simultaneously on all template samples for a single TAQMAN® PCR plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with TAQMAN® PCR primers and probe both B-actin

C7

and GAPDH on a single plate with normal human DNA and no-template controls. The diluted samples were used provided that the Ct value of normal human DNA subtracted from test DNA was ± 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough for 8-9 plates or 64 tests.

Please replace the paragraph beginning at page 47, line 5 with the following rewritten paragraph:

C8

Table 6 describes the epicenter markers that were employed in association with CT-1 (DNA58125). These markers are located in close proximity to DNA58125 and are used to assess the amplification status of the region of chromosome 16 in which DNA58125 is located. The distance between individual markers is measured in centirays, which is a radiation breakage unit approximately equal to a 1% chance of a breakage between two markers. One cR is very roughly equivalent to 20 kilobases. The marker SHGC-36123 is the marker found to be the closest to the location on chromosome 16 where DNA58125 most closely maps. However, the TAQMAN® PCR primers and probes for SHGC-2726 failed in our assay due to technical difficulties related to PCR.

In the Claims:

Claims 1, 3, 24-35 are pending in the application.

Claims 1, 25, 27-30, 33, and 35 are amended to read as follows:

C9

1. A method of diagnosing tumor in a mammal, the method comprising:

(a) detecting the level of expression of a nucleic acid sequence in a test sample of tissue cells obtained from the mammal, wherein the cells are suspected of uncontrolled growth and wherein the detecting is by contacting, under high stringency conditions, nucleic acid of the test sample cells with a nucleic acid probe comprising at least 20 contiguous nucleic acid bases from DNA 58125 (SEQ ID NO:1) or its complement (SEQ ID NO:2);

FULL?